Docket No. GJH-68
Serial No. 09/856,944

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Vera Afremova
Art Unit	:	1651
Applicant	:	Hart, John Ernest
Serial No.	:	09/856,944
Filed	:	July 16, 2001
For	:	Isolated Material Having an Anti-Organotrophic Effect

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF DR JOHN ERNEST HART UNDER 37 CFR ≥1.132

Sir:

1. I am the inventor of the invention described in the above patent application.

2. I received a BSc in Zoology from the University of Sheffield in 1975 and I received a PhD in Biochemistry from the University of Surrey, Guildford, UK, in 1981.

3. The major part of my career in biochemistry has involved the identification and elucidation of hormones in humans and animals.

4. I have read and understand the patent application serial number 09/856,944 for my invention, and I have read and understand the cited references, i.e. Hart and US 4,734,398 (diZerega). The following statements recite facts evident from those respective documents.

5. The patent application relates to a compound which I will refer to as "Micrin". Micrin, which is naturally occurring, is obtainable from the blood of sheep. Micrin is inducible by the non-endogenous, synthetic compound clomiphene. Micrin is also obtainable from sheep, even when those sheep are not treated with clomiphene, as explained in the patent application.

6. Micrin is present in a plasma fraction having a nominal cutoff of 10,000 - 20,000 daltons. Clomiphene has a molecular weight below 500.

7. diZerega discloses "Follicular Regulating Protein" (hereinafter FRP). FRP is only detectable immediately downstream of an ovary which is just about to ovulate, and is not

concurrently detectable downstream of the contralateral anovulatory ovary. Micrin is detectable six-days post-oestrus (i.e. post-ovulation), downstream of both ovaries, concurrently. FRP is not detectable in anovulatory individuals. Micrin is detectable in anovulatory individuals. FRP is not detectable in peripheral blood. Micrin is detectable in peripheral blood.

8. Micrin activity is detectable in blood plasma at a time (after ovulation) and from places (downstream of anovulatory ovaries and from peripheral blood) when and where FRP activity is not detectable (diZerega, Example One, Column 8-12, notably Column 10, lines 52-60 and Column 11, lines 61-66).

9. FRP is exclusively ovarian in origin: it is secreted by granulosa cells in the ovary (see Column 11, lines 59-60 and Column 28, line 65). Micrin is produced by the ovaries and testes, and by other organs.

10. FRP inhibits gonadotropin action in the ovary. FRP therefore suppresses gonadotropin-induced regrowth of juvenile rat ovaries previously shrunken by hypophysectomy. Micrin reduces, in normal adult female rats, the masses of organs such as the heart and kidneys which are uninfluenced by gonadotropins and remote from the ovaries. It is unlikely that FRP has a downregulatory effect on such organs as the heart and kidneys, since it is an intra-ovarian gonadotropin inhibitor which does not appear in peripheral blood.

11. I infer from Fig. 18 of diZerega that FRP is not induced by clomiphene.

12. For FRP there are described potential uses in contraception and infertility. Micrin is useful in the treatment of general organ or tissue hypertrophy.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or of any patent issuing thereon.

Further declarant sayeth naught.

Signed: John Hart
Dr. John S Hart

Date: 18th July 2003